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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,350	02/15/2006	Yuzhang Wu	CCPT124975	5046

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SEATTLE, WA 98101-2347

EXAMINER

PENG, BO

ART UNIT

PAPER NUMBER

1648

NOTIFICATION DATE

DELIVERY MODE

04/01/2011

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

efiling@cojk.com

# Office Action Summary

**Application No.**

10/528,350

**Applicant(s)**

WU ET AL.

**Examiner**

BO PENG

**Art Unit**

1648

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 03 March 2011.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-3 and 5-74 is/are pending in the application.
- 4a) Of the above claim(s) 17-22, 24-53, 61 and 66-70 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 5-16, 23, 54-60, 62-65 and 71-74 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-946)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### **Continued Examination Under 37 CFR 1.114**

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 3, 2011, has been entered.
2. Claims 1-3 and 5-74 are pending. Claims 17-22, 24-53, 61 and 66-70 have been withdrawn. Claims 1-3, 5-16, 23, 54-60, 62-65 and 71-74 are examined in this Office action. The claims read on the elected species of a polypeptide sequence 1 of SEQ ID NO: 6, sequence 2 of SEQ ID NO: 23, sequence 3 of SEQ ID NO: 48, the linking peptide of AAA between sequences 1 and 2, and GGG between sequences 2 and 3, and CH<sub>3</sub>(CH<sub>2</sub>)<sub>14</sub>CO- as modifying group (Claims 7-15), an injection formulation in Claim 59, and a lyophilized liposome dosage of Claim 72.

### **Claim Rejections - 35 USC 112, second paragraph**

2. The following is a quotation of the second paragraph of 35 USC 112:  

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
3. (**New rejection**) Claim 2 is rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
4. Claim 2 is indefinite because it lacks reference sequences for the cited fragments of HBV

proteins. Since the amino acid residues and positions vary in the different HBV strains, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention without reference sequences of the cited proteins. Appropriate correction is required.

### **Claim Rejections - 35 USC 103**

5. The following is a quotation of 35 USC 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. **(Prior rejection-maintained)** The rejection of Claims 1-16, 23, 54-60, 62, 63 and 65 under 35 USC 103(a) as being unpatentable over Vitiello (US 6,322,789) and Tam (PNAS 86:9084-9088, 1989), **is maintained** for the reason of record.

7. **(Prior rejection-maintained)** The rejection of Claims 64, 65, 71 and 72 under 35 USC 103(a) as being unpatentable over Vitiello (US6,322,789) and Tam (PNAS 86:9084-9088), as applied to Claims 1-16, 23, 54-60, 62, 63 and 65 above, further in view of Schneider (US 6,333,021), **is maintained** for the reason of record.

8. **(Prior rejection-maintained)** The rejection of Claims 73 and 74 under 35 USC 103(a) as being unpatentable over Heathcote (Hepatology. 1999 Aug;30(2):531-536), in view of Tam (PNAS 86:9084-9088, 1989) and Vitiello (US6,322,789), **is maintained** for the reason of record.

In response to Declaration of Dr. Yuzhang Wu under 37 CFR 1.132

9. Dr. Yuzhang Wu's Declaration under 37 CFR 1.132, submitted on March 2, 2011, is acknowledged. In the Declaration, Dr. Wu states: "as to how many epitopes, how many kinds of epitopes and how to combine and match them in order to generate a protective immune, little is known. Thus, one cannot simply combine one epitope and another different epitope chosen from numerous reported epitopes and assert that the combination of the two epitopes is obvious. Naturally, the combination of 3 epitopes of the present invention cannot be viewed as a simple combination of the Vitiello reference and the Tam reference." (Para 4)

10. Dr. Wu further shows that peptide D1, which comprises a combination of tetanus toxoid (TT) universal T helper epitope of SEQ ID NO: 6, a CTL epitope of SEQ ID NO: 23 and a B cell epitope of SEQ ID NO: 48; caused stronger CTL response than peptide D2 (comprising SEQ ID NOs: 6 and 23) and peptide D3 (comprising SEQ ID NOs: 6 and 48). (see Para 5-10) Dr. Wu states: "Even if one were motivated to combine a Th cell epitope, a CTL epitope and a B cell epitope to generate an immunogen, an ordinary skilled artisan would have expected that Immunogen D1 comprising a Th cell epitope, a CTL epitope and a B cell epitope would have effect which was not more than the additive effects of Immunogen D2 comprising only Th epitope and CTL epitope and Immunogen D3 comprising only Th epitope and B epitope. Therefore, there was no expectation that Immunogen D1 would generate greater effect than the sum of the effect of Immunogen D2 and the effect Immunogen D3 (namely, the additive effect of Immunogens D2 and D3). See Para 11.

11. The evidence presented in the Declaration has been considered. However, the Declaration is insufficient to overcome the 103 rejection because the evidence provided is not commensurate with the scope of the claims.

12. Claim 1 is generically directed to any peptide comprising T helper, CTL and B cell epitopes from HBV. Claims 2 and 3 are directed to many peptides comprising TT universal T helper epitope plus amino acid fragments from HBV viral proteins.

13. First, it is known in the art of immunology that all T helper, CTL and B cell epitopes are needed for induced/enhanced cellular and humoral immune responses against HBV, as taught by Vitiello and Tam. One of ordinary skill in the art would expect that a peptide comprising a combination of T helper, CTL and B cell epitopes is a better immunogen than those having T cell epitopes; or B cell epitopes alone. It is also known in the art that TT universal T cell epitopes can greatly enhance the immunogenicity of HBV antigen, like HBsAg, as evidenced by Chengalvala (Vaccine 17:1035-1041; 1999). Chengalvala teaches insertion of TT universal T cell epitope into HBsAg, which inherently contains both CTL and B cell epitopes. Chengalvala shows that TT-HBsA induced anti-HBs antibody response increased 5 to 139-fold comparing to HBsAg alone; see e.g. Table 1. Since the claimed combination of peptides does not change the operability of immunogens, rather be made based on established scientific principles, one of ordinary skill in the art would expect the peptides of Claim 1 would have greater immunogenicity than those peptides having CTL or B cell epitopes alone, especially absence of evidence to the contrary.

14. Secondly, Applicant's argument that it is not predictable which specific combination of peptides would lead to an additive effect is noted. Thus, the alleged unexpected result of peptide D1 is not representative of any other random combinations of peptides recited in Claims 2-16, 23, 54-60, 62, 63 and 65. The evidence of particular peptide D1 does not address the full scope of the claims.

15. For the reasons discussed supra, Dr. Wu's Declaration is not sufficient to overcome the  
103 rejection

### **Remarks**

16. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on Tu-F, 8:30-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Zachariah Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/BO PENG/  
Primary Examiner, Art Unit 1648